# Use of a low-resistance compliant thoracic artificial lung in the pulmonary artery to pulmonary artery configuration

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**Background:** Thoracic artificial lungs have been proposed as a bridge to transplant in patients with end-stage lung disease. Systemic embolic complications can occur after thoracic artificial lung attachment in the pulmonary artery to left atrium configuration. Therefore, we evaluated the function of a compliant thoracic artificial lung attached via the proximal pulmonary artery to distal main pulmonary artery configuration.

**Methods:** The compliant thoracic artificial lung was attached to 5 sheep (63 ± 0.9 kg) in the proximal pulmonary artery to distal main pulmonary artery configuration. Device function and animal hemodynamics were assessed at baseline and with approximately 60%, 75%, and 90% of cardiac output diverted to the compliant thoracic artificial lung. At each condition, dobutamine (0 and 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was used to simulate rest and exercise conditions.

**Results:** At rest, cardiac output decreased from 6.20 ± 0.53 L/min at baseline to 5.40 ± 0.43, 4.66 ± 0.31, and 4.05 ± 0.27 L/min with 60%, 75%, and 90% of cardiac output to the compliant thoracic artificial lung, respectively ($P < .01$ for each flow diversion vs baseline). During exercise, cardiac output decreased from 7.85 ± 0.70 L/min at baseline to 7.46 ± 0.55, 6.93 ± 0.51, and 5.96 ± 0.44 L/min ($P = .82$, $P = .19$, and $P < .01$ with respect to baseline) with 60%, 75%, and 90% of cardiac output to the compliant thoracic artificial lung, respectively. The artificial lung resistance averaged 0.46 ± 0.02 and did not vary significantly with blood flow rate.

**Conclusions:** Use of a compliant thoracic artificial lung may be feasible in the proximal pulmonary artery to distal main pulmonary artery setting if its blood flow is held at less than 75% of cardiac output. To ensure a decrease in cardiac output of less than 10%, a blood flow rate less than 60% of cardiac output is advised. (J Thorac Cardiovasc Surg 2013;145:1660-6)

Lung transplantation provides the possibility of substantially increased survival for patients with end-stage pulmonary disease. Unfortunately, the demand for donor organs continues to exceed the current supply. Although changes in the donor organ allocation system have decreased waiting list mortality, there were still 266 waiting list deaths in 2008.[1] To address this issue, thoracic artificial lungs (TALs) have been proposed as a bridge to lung transplantation.

Numerous case reports have shown that long-term extracorporeal membrane oxygenation (ECMO) can be used to bridge patients to lung transplantation.[2-5] However, cannulation and the ECMO circuit could make pretransplant rehabilitation more difficult when compared with TAL use. ECMO is also associated with blood element activation, hemolysis, and platelet consumption, which can lead to increased transfusions, systemic inflammatory response, and organ system failure.[6]

Use of a paracorporeal, pumpless TAL could enhance patient mobility preoperatively, cause fewer hematologic derangements, and expedite post-transplant recovery in patients who are bridged to lung transplantation. A previous study of the BioLung TAL (MC3 Corp, Ann Arbor, Mich) in normal sheep has shown that this device is capable of providing respiratory support for a 30-day period when used in the pulmonary artery to left atrium (PA-LA) configuration.[7] Moreover, these studies demonstrated stable platelet counts and no evidence of hemolysis, suggesting better biocompatibility compared with ECMO.[7] There is no purposely designed TAL available clinically. However, 6 patients have been bridged to transplant using a Novalung ILA (Novalung GmbH, Hechingen, Germany) in a PA-LA configuration.[8-10] The PA-LA configuration can decrease the workload of the right ventricle (RV) by providing an alternate pathway for blood flow. However, potentially catastrophic systemic embolic complications, such as stroke, could occur.[9,10]

An alternative configuration, the proximal PA to distal PA (PA-PA) configuration has a low risk for systemic embolic events. This approach is limited by the increased workload of the RV having to pump sequentially through the device

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**Abbreviations and Acronyms**

CO = cardiac output
cTAL = compliant thoracic artificial lung
CVP = central venous pressure
ECMO = extracorporeal membranous oxygenation
MAP = mean arterial pressure
PA = pulmonary artery
PA-LA = pulmonary artery to left atrium
PA-PA = proximal pulmonary artery to distal pulmonary artery
pPAP = proximal pulmonary artery pressure
PVR = pulmonary vascular resistance
RV = right ventricle
TAL = thoracic artificial lung

and the native lungs. Therefore, presence of pulmonary hypertension would be a relative contraindication to this attachment configuration. However, a significant subset of lung transplant candidates with chronic respiratory insufficiency do not have pulmonary hypertension (mean PA pressure >25 mm Hg), including 69% of candidates with idiopathic pulmonary fibrosis,[11] 50% with chronic obstructive pulmonary disease,[12] and 37% with cystic fibrosis.[13]

Nonetheless, the TAL must have a stable, low resistance for this approach to be feasible. In the current study, a new compliant thoracic artificial lung (cTAL) design is examined for this setting. The cTAL uses a compliant housing with a gradual inlet in an attempt to achieve ultra-low device resistance (0.5 mm Hg/[L/min]) at all relevant ranges of blood flow through the device. We hypothesized that this device with ultra-low resistance could be attached in the PA-PA configuration and maintain normal CO at high device flow rates. If true, this would decrease adverse events from systemic emboli in patients being bridged to lung transplantation. Thus, the current study examines the hemodynamic effect of PA-PA attachment under various percentages of CO diverted through the cTAL and under simulated rest and exercise conditions.

## MATERIALS AND METHODS

### Compliant Thoracic Artificial Lung

A cTAL, consisting of a compliant Biospan (DSM PTG, Berkeley, Calif) housing and polypropylene fiber bundle, was used in this study (Figure 1). This device was designed and constructed by our research group at the University of Michigan.[14] In this device, blood flows into the inlet conduit, expands into the inlet manifold, flows through the fiber bundle, travels through the outlet manifold, and exits through the outlet conduit. To create the fiber bundle, woven mats of polypropylene fibers with a fiber diameter of 210 $\mu$m were wound into compact bundles with porosity, path length, frontal area, and surface area of 0.75, 0.038 m, 0.013 $m^2$, and 2.4 $m^2$, respectively.

### Experimental Procedure

Five male sheep averaging 63 $\pm$ 0.9 kg were used in this study. Animal numbers were based on similar previous studies.[14] All sheep received humane care in compliance with the ''Guide for the Care and Use of Laboratory Animals,'' and all methods were approved by the University of Michigan Committee for the Use and Care of Animals. Anesthesia was induced and mechanical ventilation was performed according to previous published methods.[14] A carotid arterial line and left jugular venous line were placed and then connected to fluid-coupled pressure transducers (ICU Medical, Inc, San Clemente, Calif) for the continuous monitoring of mean arterial pressure (MAP) and central venous pressure (CVP).

A muscle-sparing left anterolateral thoracotomy was performed, and the fourth rib was removed. The left lung was packed laterally, and the pericardium was incised. The pulmonary artery (PA) was then identified. Dacron vascular grafts (18 mm; Terumo Medical Corp, Ann Arbor, Mich) were solvent bonded to 5/8'' inner diameter polyvinyl chloride tubing (Fisher Scientific, Pittsburgh, Pa) and used as conduits for artificial lung attachment. An end-to-side anastomosis was performed between the device outlet conduit and the distal PA near the bifurcation. The device inlet end-to-side anastomosis was then performed on the proximal PA. An ultrasonic perivascular flow probe (Transonic 24AX, Transonic Systems, Inc, Ithaca, NY) was placed around the PA, proximal to the device inlet graft for measurement (T400, Transonic Systems) of mean PA flow or cardiac output (CO). A pressure catheter (Becton Dickinson and Co, Franklin Lakes, NJ) was then inserted at the proximal PA and connected to a transducer for the display and recording of the proximal PA pressure (pPAP). A Rummel tourniquet was placed around the PA between the inlet and outlet grafts to allow for the adjustment of flow through the cTAL. Pressure catheters were inserted into the distal PA near the bifurcation and into the left atrium to allow for the recording of the distal PA pressure and the left atrial pressure. Before device attachment, 1g of methylprednisolone (Solu-Medrol; Pfizer, New York, NY) was administered, and the animal was anticoagulated with 100 IU/kg of intravenous sodium heparin (Baxter Healthcare Corp, Deerfield, Ill) to maintain active clotting times greater than 300 seconds.

The cTAL was primed with heparinized saline (10 U/mL) and then connected to the proximal PA (device inlet) and distal PA (device outlet) grafts (Figure 2). An ultrasonic flow probe (Transonic 14PXL; Transonic Systems, Inc) was placed around the inflow conduit to measure (T400; Transonic Systems Inc) device flow ($Q_{cTAL}$). The cTAL inlet and outlet pressures ($P_{in}$ and $P_{out}$) were measured by fluid-coupled pressure transducers. A suction line was attached to the cTAL gas outlet, and 95:5% $O_2$:$CO_2$ with vaporized isoflurane (1%-3%) was used as the sweep gas through the gas inlet. Sweep gas flow was adjusted during cTAL use to maintain the arterial carbon dioxide tension between 35 and 45 mm Hg. A Hoffmann clamp was placed around the cTAL outlet conduit to restrict flow through the device. After cTAL attachment, the clamps on the cTAL inlet and outlet conduits were removed, and the Hoffmann clamp was loosened until 1 L/min flow to the cTAL was achieved. This flow was maintained for 10 minutes for equilibration of fluid volumes and any inflammatory response. Flow to the cTAL was then stopped briefly, and up to 500 mL of hetastarch and 500 mL of crystalloid were administered to restore CVP back to pre-cTAL values, if required.

Rest and exercise conditions were then simulated using a continuous dobutamine (Hospira Inc, Lake Forest, Ill) infusion of 0 and 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$, respectively. At each dose, a data set was acquired at baseline, with no flow to the device. Thereafter, the clamps were removed from the cTAL and the Rummel tourniquet was tightened to divert 60%, 75%, and 90% of CO to the cTAL. At each condition, 10 minutes were allowed for equilibration before data were taken. A data set consisted of recording the average values of all blood pressures and flows. In addition, arterial and device inlet and outlet blood samples were taken and assayed for pH, carbon dioxide tension, and oxygen tension using an ABL 725 blood gas analyzer (Radiometer Copenhagen, Copenhagen, Denmark).

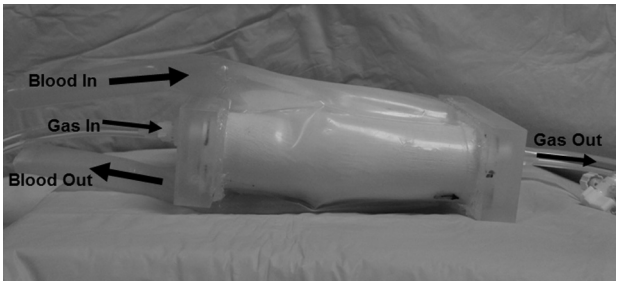


**FIGURE 1.** The cTAL demonstrating the blood and gas flow paths.

## Data Analysis

Average blood flows and pressures were used to calculate all resistances. The CO is equal to the average PA flow rate. cTAL resistance, $R_{cTAL}$, was calculated using the following formula:

$$R_{cTAL} = \frac{P_{in} - P_{out}}{Q_{cTAL}}. \quad (1)$$

The pulmonary vascular resistance (PVR) of the native lungs was calculated by the following formula:

$$PVR = \frac{dPAP - LAP}{CO}. \quad (2)$$

The resistance of the graft anastomoses, $R_a$, was calculated by analyzing all the resistive elements in the experimental pulmonary system setup (Figure 2). Total pulmonary system resistance, $R_T$, is defined as the resistance of combined artificial and natural lung system from the proximal PA to the left atrium, and is thus calculated as follows:

$$R_T = \frac{pPAP - LAP}{CO}. \quad (3)$$

Shunt resistance, $R_s$, is defined as the resistance of the section of the main PA containing the artificial lung and its anastomoses, which is in series with the natural lungs. It was thus calculated as follows:

$$R_s = R_T - PVR. \quad (4)$$

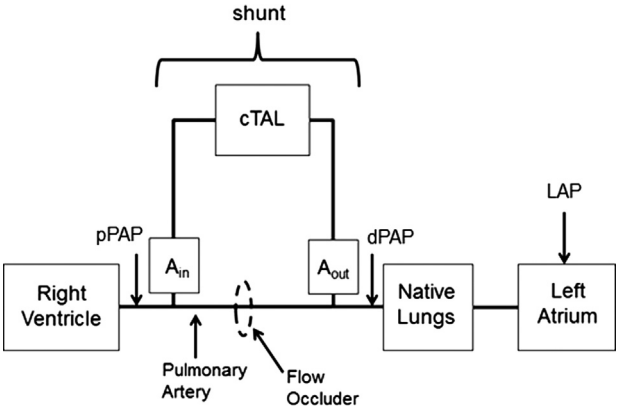


**FIGURE 2.** Experimental pulmonary system setup with all resistive elements. The shunt includes the anastomoses ($A_{in}$ and $A_{out}$), the cTAL, and the flow occluder. *cTAL,* Compliant thoracic artificial lung; *pPAP,* proximal pulmonary artery pressure; $A_{in}$, inlet anastomosis; $A_{out}$, outlet anastomosis; *dPAP*, distal pulmonary artery pressure; *LAP*, left atrial pressure.

The sum of the anastomoses resistances, $R_a$, is assumed to be in series with the cTAL resistance, giving the following relationship:

$$R_a = \frac{R_s}{f} - R_{cTAL}, \quad (5)$$

In which $f$ is the fraction of $CO$ diverted to the cTAL. The values of $R_T$, $R_s$, and $R_a$ were thus calculated at each flow condition.

Statistical analyses were performed using the Statistical Package for the Social Sciences version 19 (SPSS, Inc, Chicago, Ill). The analysis of baseline PVR before and after TAL attachment was conducted using a paired 2-tailed Student $t$ test assuming equal variances. To examine whether cTAL resistance varied significantly with flow rate, a 1-way analysis of variance was performed. For comparisons of mean values of all other dependent variables, linear models with correlated error structures (given the repeated measures) were fitted to the observed data. Separate models were fitted for the 0 and 5 $\mu$g/kg/min of dobutamine data. Each model included fixed effects of flow diversion to examine differences between baseline and 60%, 75%, and 90% flow diversion. Alternative covariance structures were compared using information criteria (eg, Akaike information criterion, Bayesian information criterion). In most cases, an autoregressive covariance structure was found to have the best fit. However, Toeplitz and diagonal covariance structures were used for PVR and mean pulmonary artery pressure, respectively. A Bonferroni correction was applied to the contrasts to prevent increases in type I error rates. All data are reported as the mean $\pm$ the standard error.

# RESULTS

## Device Function

The resistance of the cTAL did not change significantly with flow rate ($P = .16$), averaging 0.46 $\pm$ 0.02 mm Hg/(L$\cdot$min$^{-1}$) over the entire range of flows. Because of the relatively high venous saturations (83.1% $\pm$ 1.3%) and lower hemoglobin (6.11 $\pm$ 0.17 g/dL), the gas transfer function of the lung was never challenged. Arterial blood gas hemoglobin oxygen saturations were maintained at 99% for all of the conditions. Finally, all of the devices functioned without a noticeable decrease in gas exchange or increase in resistance. There was no noticeable clot formation within the device at the conclusion of the experiment.

## Sheep Hemodynamics

During the early equilibration period, there was an event due to blood contact with the artificial lung featuring increased PVR and decreased MAP and CO. This is common to blood-bearing artificial circuits and is normally attributed to inflammation.[6] During this event, PVR increased from 1.61 $\pm$ 0.32 mm Hg/(L/min) to 3.13 $\pm$ 0.17 mm Hg/(L/min) ($P = .01$), CO decreased from 6.58 $\pm$ 0.56 L/min to 6.20 $\pm$ 0.53 L/min, and MAP decreased from 87.6 $\pm$ 6.2 to 80.9 $\pm$ 3.9.

Thereafter, CO was 6.20 $\pm$ 0.53 L/min at the experimental baseline and decreased 13% to 5.40 $\pm$ 0.34 L/min at 60% flow to the cTAL ($P < .01$), 25% to 4.66 $\pm$ 0.31 L/min at 75% flow to the cTAL ($P < .01$), and 35% to 4.05 $\pm$ 0.27 L/min at 90% flow to the cTAL ($P < .01$) (Figure 3, *A*). After starting dobutamine at 5 $\mu$g$\cdot$kg$^{-1}\cdot$min$^{-1}$, CO increased to 7.85 $\pm$ 0.70 L/min at

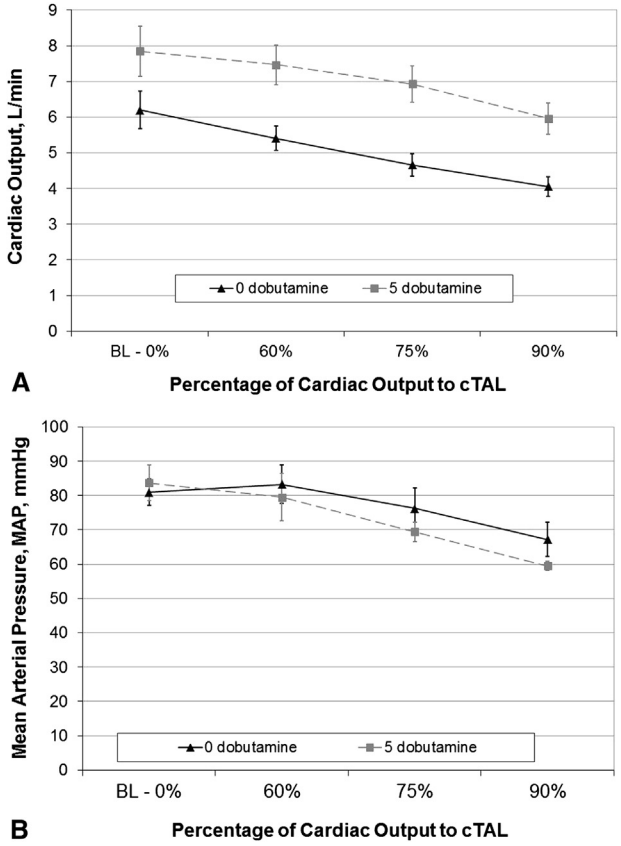


**FIGURE 3.** CO (A) and MAP (B) versus the percentage of CO shunted to the compliant artificial lung for dobutamine doses of 0 $\mu$g/kg/min and 5 $\mu$g/kg/min. *BL,* Baseline; *cTAL,* compliant thoracic artificial lung; *MAP,* mean arterial pressure.

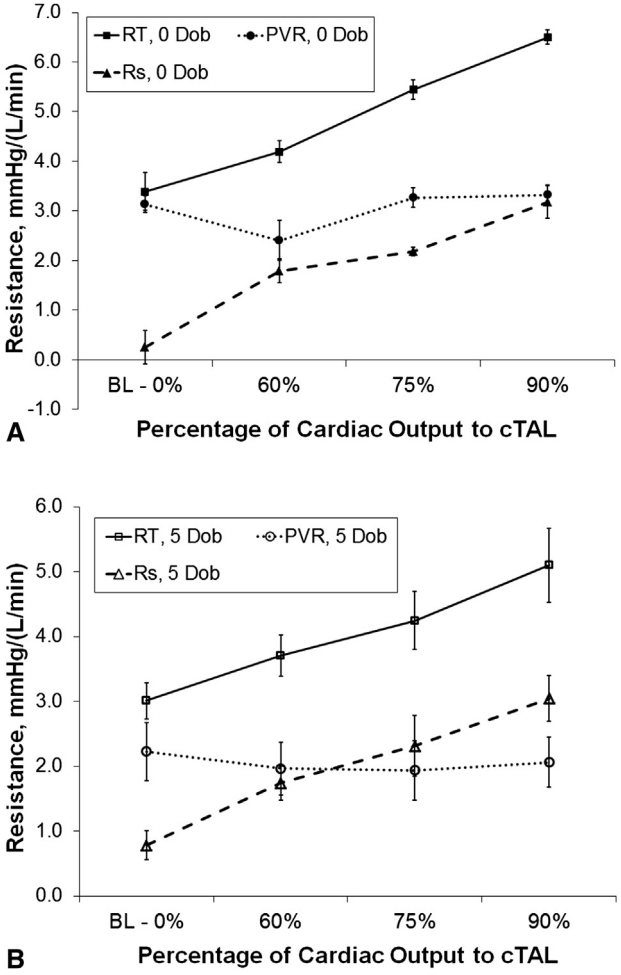


**FIGURE 4.** Total pulmonary system resistance, PVR, and shunt resistance at varying percentages of CO diverted to the compliant artificial lung for dobutamine doses of (A) 0 $\mu$g/kg/min and (B) 5 $\mu$g/kg/min. *RT,* Total pulmonary system resistance; *Rs,* shunt resistance; *Dob,* dobutamine; *PVR,* pulmonary vascular resistance; *BL,* baseline; *cTAL,* compliant thoracic artificial lung.

baseline with no flow to the cTAL. Once again, CO decreased with increasing flows to the cTAL, decreasing 5% to 7.46 $\pm$ 0.55 L/min ($P = .82$), 12% to 6.93 $\pm$ 0.51 L/min ($P = .19$), and 24% to 5.96 $\pm$ 0.44 L/min ($P < .01$) with 60%, 75%, and 90% of CO going through the cTAL, respectively. Other measures of RV dysfunction varied only slightly and were not as sensitive as CO. The CVP was between 11.4 and 12.5 mm Hg under all conditions and did not change significantly with attachment mode at 0 or 5 $\mu$g/kg/min of dobutamine ($P = .08$ and $P = .59$). Lactate was within normal ranges for the duration of the experiment (0.8-1.4 mmol/L). The only statistically significant change was a decrease in lactate with increasing flow the cTAL with 0 dobutamine ($P < .01$ vs baseline).

The MAP decreased with increasing flow to the TAL (Figure 3, *B*), as did CO. The baseline MAP was 81 $\pm$ 4.0 mm Hg and increased slightly to 83 $\pm$ 5.7 mm Hg at 60% of cTAL flow ($P = .99$) before decreasing to 76 $\pm$ 6.1 mm Hg ($P = .88$) and 67 $\pm$ 5.0 mm Hg ($P < .05$) under 75% and 90% cTAL flow conditions, respectively. Under the simulated exercise condition, the baseline MAP was 84 $\pm$ 5.3 mm Hg. This decreased to 80 $\pm$ 6.9 mm Hg at 60% cTAL flow ($P = .99$), 69 $\pm$ 2.8 mm Hg at 75% flow to the cTAL ($P < .05$), and 60 $\pm$ 1.3 mm Hg at 90% flow to the cTAL ($P < .01$).

The cause of diminishing CO and MAP with increasing flow diversion to the cTAL is increasing RV afterload. Figure 4 shows the total pulmonary system resistance ($R_T$) and its 2 subsections, shunt resistance ($R_s$) and PVR. As blood flow is diverted to the cTAL, $R_T$ increases linearly at both 0 and 5 $\mu$g/kg/min of dobutamine from 3.39 $\pm$ 0.38 and 3.01 $\pm$ 0.28 mm Hg/(L/min) at baseline to 6.50 $\pm$ 0.14 and 5.10 $\pm$ 0.57 mm Hg/(L/min) at 90% flow to the cTAL. The PVR does not change significantly with flow diversion ($P = .21$, .99, and .99 with increasing cTAL flow in the 0 dobutamine conditions and $P = .35$,

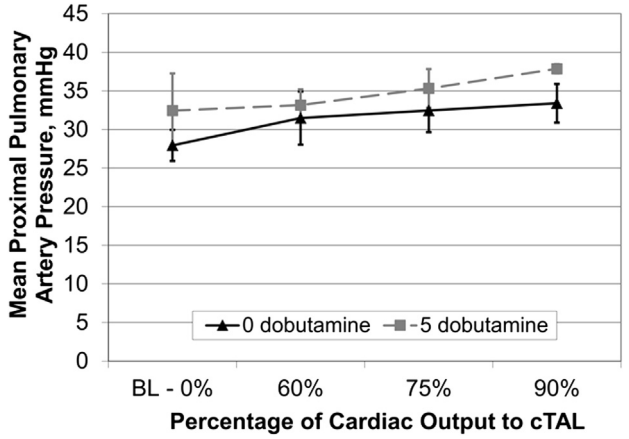


**FIGURE 5.** Mean pPAP versus the percentage of CO shunted to the compliant artificial lung for dobutamine doses of 0 $\mu$g/kg/min and 5 $\mu$g/kg/min. *BL,* Baseline; *cTAL,* compliant thoracic artificial lung.

.59, and .99 during the 5 $\mu$g/kg/min of dobutamine conditions). However, as the PA is banded, blood flows increasingly through the higher resistance circuit with the TAL and its anastomoses. As a result, $R_s$ increases from 0.26 $\pm$ 0.34 and 0.78 $\pm$ 0.22 mm Hg/(L/min) at baseline to 3.18 $\pm$ 0.32 and 3.04 $\pm$ 0.35 mm Hg/(L/min) with 90% of CO going to the TAL with 0 and 5 $\mu$g/kg/min, respectively. Finally, the increased resistance was due to increased flow through this high-resistance circuit and not due to changes in the resistances themselves. Neither $R_{cTAL}$ nor $R_a$ changed significantly with increasing flow diversion ($P = .42$ and $P = .11$ at 0 $\mu$g/kg/min dobutamine and $P = .42$ and $P = .35$ at 5 $\mu$g/kg/min dobutamine for $R_{cTAL}$ and $R_a$, respectively). The $R_a$ was 2.63 $\pm$ 0.43, 2.39 $\pm$ 0.17, and 3.06 $\pm$ 0.37 mm Hg/(L/min) at 60%, 75%, and 90% diversion at 0 $\mu$g/kg/min of dobutamine, respectively, and 2.25 $\pm$ 0.54, 2.60 $\pm$ 0.63 mm Hg/(L/min), and 2.88 $\pm$ 0.39 mm Hg/(L/min) with 60%, 75%, and 90% diversion at 5 $\mu$g/kg/min of dobutamine, respectively.

Because of offsetting changes in CO and $R_T$, pPAP increased only a small amount with increasing flow diversion (Figure 5). Baseline pPAP was 28 $\pm$ 2.0 mm Hg and increased by a statistically insignificant amount ($P = .16$) to 33 $\pm$ 2.5 mm Hg at 90% flow to the cTAL with 0 $\mu$g/kg/min of dobutamine. In a similar fashion, the baseline pPAP of 32 $\pm$ 4.8 mm Hg increased insignificantly ($P = .98$) to 38 $\pm$ 0.6 mm Hg at 90% flow to the cTAL with 5 $\mu$g/kg/min of dobutamine.

## DISCUSSION

Several previous studies have examined TAL use in a PA-PA setting. Lick and colleagues[15] used an early prototype of the MC3 BioLung in conscious, normal sheep with 100% flow diversion, resulting in poor heart function, including a 50% incidence of right heart failure.[15] In surviving sheep, however, heart function improved over the 7-day study. Thereafter, the BioLung was redesigned to reduce blood-flow impedance. The result was a device with an average blood flow resistance of approximately 1.8 mm Hg/(L/min) under simulated blood flow conditions.[16] Subsequently, this device was tested in conscious sheep with acute respiratory distress syndrome, again with 100% diversion. This study demonstrated an approximate 20% decrease in CO, followed by accommodation and normalization of CO.[17] Sato and colleagues[16] tested the MC3 BioLung in anesthetized sheep and found a 25% decrease in CO with 100% flow diversion. Perlman and colleagues[18] also tested an early cTAL prototype in 2 groups of anesthetized pigs with 42% or 100% flow diversion. This device had an average blood flow resistance of 1.9 mm Hg/(L/min) under the same conditions as the BioLung.[19] In this setting, CO decreased by 12% and 42%, respectively.

The goal of the current study was to determine whether further hemodynamic improvements in PA-PA attachment were possible using newer, ultra-low impedance TALs. In vitro studies of this device indicate that resistance is 0.53 $\pm$ 0.06 mm Hg/(L/min) at blood flows of 4 L/min, and compliance was 5.21 $\pm$ 0.57 mL/mm Hg.[1] This resistance was less than one third of previously published devices, and the compliance was 18% greater than previous designs.[16,19,20] This study confirmed that it is possible to achieve PA-PA attachment with both significant TAL flow and minimal impact on hemodynamics. However, CO decreased 25% and 12% during rest and exercise conditions at 75% diversion. As a result, diversion of 60% of CO or less seems to be a more reasonable level. At 60%, there was a 13% and 8% decrease in CO at rest and exercise conditions, respectively. This is a level to which the heart could likely accommodate (see next page).

The CO decrease in the present study is similar to that in the studies by Sato and colleagues[16] and Perlman and colleagues,[18] despite lower TAL and pulmonary system resistances. Those studies demonstrated a 4 mm Hg/(L/min) increase in pulmonary system resistance at 100% flow diversion versus approximately 3.1 mm Hg/(L/min) at 90% diversion in the current study. A pulmonary system resistance reduction of 0.9 mm Hg/(L/min) should lead to a 5% to 7% increase in CO,[21,22] or only 0.3 to 0.4 L/min. Thus, the benefits gained from even a large decrease in TAL resistance are small. Ultimately, the largest resistance in the system is not the cTAL itself, but that of the anastomoses. Anastomoses resistances averaged approximately 2.6 mm Hg/(L/min) in the current study, similar to that of previous studies,[16,21] whereas the cTAL resistance is now only 0.5 mm Hg/(L/min).

Despite the limited improvement in CO, minimization of TAL resistance should remain the goal to minimize RV strain. Three groups have reported on the use of the Novalung

lung assist device in a PA-LA configuration in 7 patients with marked pulmonary hypertension.[8-10] Average device flow in these patients ranged from 2.5 to 3.0 L/min with a pressure decrease of 25 to 30 mm Hg across the device, or a device resistance of 10 mm Hg/(L/min).[10] Although this still allowed modest RV unloading in the PA-LA setting, this device would not be tolerated in a PA-PA configuration.

Despite these limitations, long-term results in conscious subjects should be significantly better. Two previous studies have indicated improved CO over 3 to 7 days of PA-PA support in conscious sheep with 100% flow diversion.[16,17] This may be due to RV accommodation or alleviation of the effects of both anesthesia and any inflammatory response to the device. Prolonged anesthesia leads to a progressive decrease in MAP, RV perfusion, and thus CO.[23,24] There was also an initial event that increased PVR and most likely a loss in cardiac function before the experimental period beginning.[6,23] These events are common to blood contact with any blood gas exchanger, be it cardiopulmonary bypass, ECMO, or the cTAL and are typically attributed to inflammation.[6] This effect typically resolves within 24 hours after initiation of ECMO,[25,26] and there is no evidence of a significant systemic inflammation within 24 hours after TAL attachment.[7] Thus, as arterial pressure returns to normal and the inflammation abates, cardiac function is likely to improve in awake sheep.

As stated earlier, the ability of the device to transfer oxygen was never challenged because of the use of 100% inspired oxygen and low hemoglobin. As a result, device outlet oxygen saturation was always greater than 99%. Gas exchange function for this device has recently been described under more challenging conditions.[14] In that study, inlet blood conditions were set to those from the Food and Drug Administration "Guidance for Cardiopulmonary Bypass Oxygenators 510(k) Submissions" and the standards provided by American National Standards Institute/Association for the Advancement of Medical Instrumentation/International Organization for Standardization 7199.[27,28] These were, in part, hemoglobin = 12 ± 1 g/dL, oxygen saturation = 65% ± 5%, and carbon dioxide tension = 45 ± 5 mm Hg. With these inlet conditions, outlet oxyhemoglobin saturation was greater than 99% and partial pressure of oxygen was at least 243 mm Hg with up to 7 L/min of blood flow. The resulting oxygen transfer at 7 L/min was 395 mL/min. The $CO_2$ transfer was not examined. However, $CO_2$ transfer is typically excessive in these devices, requiring $CO_2$ to be added into the sweep gas.[7] This level of gas transfer is more than sufficient for this application.

## CONCLUSIONS

The cTAL tested in the current study had a resistance well below previous TALs at all flow rates tested and maintained adequate gas exchange under all conditions. Despite this, flow diversion to the device should be limited to less than 60% of CO in the PA-PA setting to minimize changes in pulmonary hemodynamics. However, further study is required to determine the effect of PA-PA attachment in conscious sheep. Ultimately, if the cTAL can be used in the PA-PA configuration with minimal alteration in hemodynamics, systemic embolic complications could be eliminated.

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